PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group Art Unit: 1632

Examiner: Anne Marie Sabrina Wehbe

In re application of:
Alain P. Vicari *et al.*

Serial No.: 09/768,917

Filing Date: January 24, 2001

Attorney Docket No.: SF0896 K US

Title:
CHEMOKINES AS ADJUVANTS OF IMMUNE RESPONSE

DECLARATION UNDER 37 C.F.R. § 1.132

I, Alain P. Vicari, hereby declare as follows:

1. I am a named inventor in the above-refereniced patent application. I am informed that the claims in the above-referenced patent application have been amended to recite a method for enhancing an immune response in a mammal comprising administering an antigen and a chemokine to the mammal, wherein the chemokine is MCP-4 or a biologically active fraction of MCP-4, and wherein the antigen and the chemokine are not physically linked as a fusion protein.

2. Furthermore, I am informed that Schering-Plough Corporation received two Office Actions having mailing dates of July 30, 2003 and December 22, 2003 in the above-referenced application. I have also been informed that the Office Actions reject claims 21-24, 26-36 and 69 under 35 U.S.C. § 103(a) as being unpatentable over European Patent Application Publication No. EP 0 974 357 A1 ("Caux"), in view of PCT International Application Publication No. WO 98/14573 ("Luster") and a journal article by Dieu-Nosjean *et al.*, "Regulation of dendritic cell trafficking: a process that involves the participation of selective chemokines", *J. Leukocyte Biology*, vol. 66, pp. 252-262 (1999) ("Dieu-Nosjean").

3. I am a named inventor of Caux and have read and understand its contents. Caux relates generally to the use of chemokines to modulate immune responses. The disclosure is specifically directed to the chemokines MIP-3α and MIP-3β.

4. I have also read and understand the contents of the Luster and the Dieu-Nosjean references. Luster relates to the use of MCP-4 for enhancing an immune response while the Dieu-Nosjean reference is a review article relating to dendritic cells and dendritic cell trafficking.

5. It is my view that even if, for argument sake, an ordinary skilled scientist working in the field related to the subject matter of this application would have been motivated to substitute MCP-4 for MIP-3α, as suggested by the Examiner, that scientist would not have

PAGE 12/14 * RCVD AT 1/30/2004 4:20:40 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/6 * DNIS:8729307 * CSID:908 298 5405 * DURATION (mm-ss):03-56

expected to see the dramatic increase in immune response demonstrated in the instant specification when MCP-4 is employed in conjunction with an antigen (see, for example, Figures 3-7 of the instant specification).

6. In support of this view, I am submitting herewith as Exhibit A data derived from an experiment wherein the antigen specific humoral immune response of MCP-4 and MIP-3α were directly compared. In this experiment, groups of seven mice were injected in the right hind footpad with either 100 ng of recombinant human MIP-3α protein (hMIP-3α) or 100 ng of recombinant human MCP-4 protein (hMCP-4) in 50 μl of PBS. After three hours, the mice were injected at the same site with either 50 μg of a control plasmid (pCDNA3) or 50 μg of pCDNA3 plasmid encoding for β-galactosidase under the CMV promoter (pLacZ). Serum was collected both one day before the first immunization and at day 28 after four weekly immunizations. The serum levels of β-galactosidase specific immunoglobulins were measured using ELISA.

7. In my view, the data shown in Exhibit A clearly demonstrates that hMCP-4 injection increases the antigen specific humoral immune response following DNA immunization, whereas hMIP-3α injection does not. In fact, the data in Exhibit A shows that hMIP-3α does not exhibit any increased effect over the control plasmid pLacZ.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statement were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under 18 U.S.C. § 1001 and that such willful false statement may jeopardize the validity of the application and any patent issued thereon.

Alain P. Vicari

January 30, 2004
Date

PAGE 13/14 * RCVD AT 1/30/2004 4:20:40 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/6 * DNIS:8729307 * CSID:908 298 5405 * DURATION (mm-ss):03-56

014
SCHERING-PLOUGH
01/30/04 17:27 FAX 908 298 5405

MCP-4 but not MIP-3a injection increases the antigen-specific humoral response following DNA immunization (50 micrograms pLacz DNA injection 3 hours after 100 ng hMCP-4 or hMIP-3α recombinant protein injection in the rear right footpad).
Figure shows anti-betagalactosidase antibodies titration in serum measured prior or after 4 weekly immunizations (Day 28) in groups of seven mice.

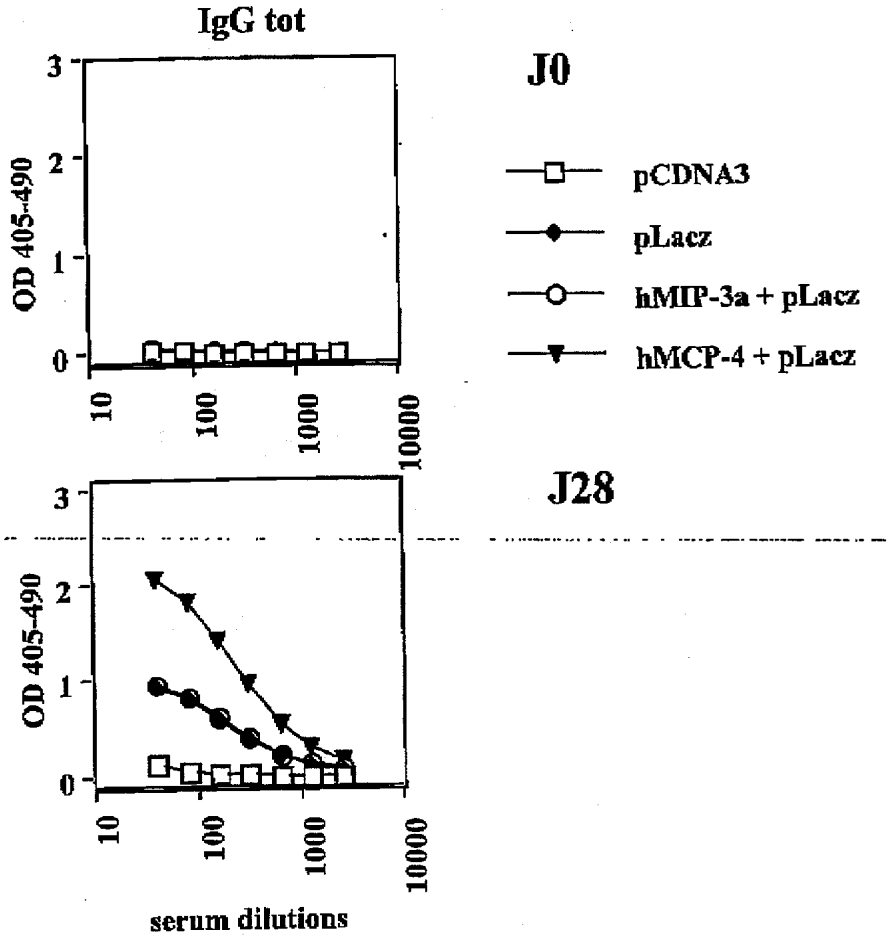

Exhibit A

PAGE 14/14 * RCVD AT 1/30/2004 4:20:40 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/6 * DNIS:8729307 * CSID:908 298 5405 * DURATION (mm-ss):03-56